REMARKS

With entry of the present amendment, claims 1 to 3 and 13 to 17 are pending. Claims 4 to 12 have been canceled without prejudice. No new claims have been added. Claims 1 to 3 have been amended and claims 13 to 17 have been added. No new matter is believed to be presented by the foregoing amendments.

Claim 1 was amended to more particularly define the mRNA to be detected as being one which is capable of being used in the production of the sequence consisting of SEQ ID NO: 1. This is consistent with what the Examiner considers to be the scope of an enabled embodiment of the invention and one which has written descriptive support in the specification. Support for this amendment is found in paragraph [0021] of the specification as filed. In a previous October 11, 2007 Amendment which was not entered, applicants had amended the claim to define the mRNA as being one which is capable of producing the cDNA consisting of SEQ ID NO: 1. The Examiner correctly noted that mRNA, by itself, is not capable of producing such cDNA. Applicants had intended to define the mRNA as being one which is capable of being used in the production of the sequence consisting of SEQ ID NO: 1 and the claim has now been amended accordingly.

Claim 2 was amended to more particularly define the process therein as being one for use in determining whether or not a test sample contains pancreatic tumor cells. Support for this amendment is in the claim as originally filed.

Claim 2 was also amended to specify that the step of comparison between the level of hybridization in the test sample and the level of hybridization in a second sample involve identifying whether the test sample contains an approximately 15-fold to approximately 60-fold greater level of hybridization as compared with the test sample. Support for this amendment is in paragraph [0029] of the specification as filed.

Claim 3 was amended to specify that the step of comparison between the level of hybridization with a probe in a test sample and the level of mRNA of a housekeeping gene involve identifying whether the level of mRNA encoding UKW in the sample is at least 3-fold greater that the level of mRNA of the housekeeping gene. Further, the claim was amended to recite that the level of mRNA encoding UKW is evidenced by the approximate amount of hybridization of the test sample with the probe and to clarify that the level of mRNA of housekeeping gene to be measured is the level present in the same test sample. Support for this amendment is in paragraph [0029] of the specification as filed.

Claims 2 and 3 were further amended to define the nucleic acid which is capable of hybridizing under stringent hybridization conditions with the nucleic acid consisting of SEQ ID NO: 1, a fragment thereof, and/or a nucleic acid which is 100% complementary to such sequences, as being one which is capable of hybridizing under high stringent hybridization conditions to such sequences. Support for this amendment is in paragraph [0024] of the specification as filed.

In addition to the above, claim 2 was amended to clarify that the nucleic acid of SEQ ID NO: 1 is a nucleic acid which consists of SEQ ID NO: 1 and claims 2 and 3 were amended to clarify that the nucleic acid which is complementary to SEQ ID NO: 1 or a fragment thereof is one which is 100% complementary thereto. Applicants maintain that this amendment does not substantively change the claims since one skilled in the art would recognize that "a nucleic acid of SEQ ID NO: 1" is one which consists of SEQ ID NO: 1 and a nucleic acid which is complementary to a particular sequence is one which is 100% complementary to that sequence.

Amendments of an editorial nature were also made to claim 3.

Claims 13 to 15 have been added to further define the invention as defined by claim 2. Support for these claims is in claim 2 as filed originally.

Claims 16 and 17 have been added to further define the invention as defined by claim 3. Support for these claims is in claim 3 as filed originally.

The Priority Document

In her previous Action, the Examiner alleged that the certified copy of the European patent application serving as the priority document for the present application provided to the Patent Office did not relate to the present invention. As such, the Examiner advised that she was not going to recognize the filing date thereof as being the priority date. In applicants' previous Reply, applicants advised that they would investigate this matter.

Applicants have since duly investigated this matter and found that a correct certified copy of European Application No. 02024539.5 was indeed filed in the Patent Office on November 8, 2004, as evidenced by a return postcard from the Patent Office confirming safe receipt thereof, and that this application does, in fact, relate to the present invention. Applicants filed a Communication advising of this on May 24, 2007. However, the Examiner has not addressed this Communication in her present Action.

Applicants are willing to file a second certified copy of the application if necessary. However, as the Patent Office has already confirmed safe receipt of the first copy, applicants respectfully submit that any confusion as to whether the copy filed relates to the present invention was likely either caused by a clerical error on the part of the Patent Office (e.g., matching the wrong priority document with the present case) or by a misreading of the priority document. Until the Office considers the aforementioned Communication, applicants will not know whether it is necessary to provide a second certified copy of the application. Applicants, therefore, respectfully request that the Examiner fully consider the Communication and respond thereto.

The Section 112, Enablement Requirement, Rejections

Claims 1 to 3 were rejected under the enablement requirement of Section 112, first paragraph.

Claim 1 was rejected because the specification allegedly does not enable one skilled in the art to use the assay when the mRNA to be detected is an mRNA other than that which is useful in producing the cDNA of SEQ ID NO: 1. According to the Examiner, "there is no teaching in either the specification or the art or record that any mRNA other than that which is useful to produce the cDNA consisting of SEQ ID NO: 1, is in any way associated with pancreatic cancer." While not acquiescing in the Examiner's rejection, applicants have hereby amended claim 1 to define the mRNA to be detected by the claimed assay as being one which is capable of being used in the production of the sequence consisting of SEQ ID NO: 1. In view of the above, the Examiner's rejection of claim 1 has been overcome.

Claim 2 and 3 were rejected because the application allegedly does not provide enablement for the use of all of the probes recited for use in the process encompassed by the claims. The Examiner alleges that the specification does not enable, for use as probes, a sequence complementary to SEQ ID NO: 1 or a fragment thereof other than one which is 100% complementary thereto or all of the probes in the full range of possible sequences which are capable of hybridizing under moderate hybridization conditions with SEQ ID NO: 1 or a fragment thereof. While not acquiescing in the Examiner's rejection, applicants have hereby amended claims 2 and 3 to more specifically define the probe which is complementary to SEQ ID NO: 1 (or a fragment thereof) as being one which is 100% complementary thereto and to specify that the hybridization conditions with regard to the second set of probes be high stringency. As such, the Examiner's rejection has been overcome.

Claims 2 and 3 were further rejected because the Examiner alleges that the specification does not enable the practice of a process for use in determining whether a test sample contains pancreatic tumor cells of fluid therefrom "in the absence of a predictable and reliable decision line/cut-off point for determining the presence or absence of pancreatic cancer" (quoting from the rejection as presented in her February 6, 2007 Action, the rejection being repeated in the current Action). While not acquiescing in the Examiner's rejection, applicants have hereby amended claim 2 to recite that an approximately 15-fold to approximately 60-fold difference in the level of hybridization present in the test sample as compared with the level of hybridization present in the control sample is indicative of the presence of pancreatic tumor cells. In addition, claim 3 has been amended to recite that an at least 3-fold difference in the level of hybridization present in the test sample (one skilled in the art would recognize that the level of hybridization present in a test sample when a probe for UKW is incubated with the sample is indicative of the level of mRNA encoding UKW) as compared with the level of mRNA of a housekeeping gene present in the sample is indicative of the presence of pancreatic tumor cells. In view of the above, this rejection has been overcome.

Claim 3 was further rejected because the specification allegedly does not enable a process for detecting pancreatic tumor comprising comparing the level of mRNA which codes for the cDNA of SEQ ID NO: 1 in a sample to the level of mRNA of a housekeeping gene in the same sample. The Examiner claims that "no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the claimed method would function as claimed with a reasonable expectation of success." The Examiner also states, without any basis, that "no one of ordinary skill in the art would believe it more likely than not that one could differentiate any tumor from normal cell

[sic] simply by comparing a tumor marker mRNA to a housekeeping gene from the same cell." The Examiner's rejection is respectfully traversed.

In the first instance, applicants note that the MPEP provides that the "lack of working examples or lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement." MPEP §2164.04.

In addition to the above, MPEP §2164.04 specifically states the following (emphasis added).

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, **unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support**.

MPEP §2164.04 also provides that "[i]n order to make a rejection, **the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention**" (emphasis added). In the present instance, the specification teaches that an at least 3-fold difference in the level of hybridization present in the test sample as compared with the level of mRNA of a housekeeping gene in the same test sample (i.e., not in a control) is indicative of the presence of pancreatic tumor cells (see paragraph [0029] of the specification as filed). In the present case, the sole reason provided by the Examiner for questioning this teaching respecting the practice of the claimed invention is that Example 1 allegedly contradicts the aforementioned teaching of the specification. The Examiner states "[o]ne cannot extrapolate the teaching of the specification to the enablement of the scope of the claim because it is clear that the specification as originally filed presents contradictory

information." According to the Examiner, Example 1 allegedly discloses a different assay, one in which the levels for mRNA coding for the cDNA of SEQ ID NO: 1 and mRNA of a housekeeping gene present in a test sample were compared with the levels of mRNA for the cDNA of SEQ ID NO: 1 and mRNA of a housekeeping gene present in a control sample. The Examiner claims that "it appears that whoever wrote the body of the specification did not understand the claimed invention" and concluded that "it is clear that the claimed invention is not practiced with a comparison to a normal control in order to detect the presence of pancreatic tumor." Applicants submit that this basis -- the sole reason offered for questioning the enablement provided in the specification -- is in error.

By way of background, applicants' invention resides in the discovery that the UKW gene is upregulated in pancreatic tumor cells in comparison to the UKW gene in non-cancerous cells and in comparison to housekeeping genes which are not upregulated in pancreatic tumor cells.

One aspect of the present invention relates to an assay for determining whether pancreatic tumor cells are present in a test sample by comparing the level of UKW-encoding nucleic acid present in the test sample with the level of UKW-encoding nucleic acid present in a sample known to not have pancreatic tumor cells (the control sample). This assay is defined by claim 2 of the present application. In the practice of this assay, one skilled in the art would know that a straight comparison of the absolute values for levels of UKW nucleic acid present in each sample might not be scientifically correct. This is because differing conditions in one sample versus the conditions in the second sample may lead to an upregulation of all genes, including housekeeping genes. To account for this, the levels of nucleic acid encoding housekeeping genes present in each sample may also be measured and the values of the UKW nucleic acid levels in each sample normalized against the values for the nucleic acids for the housekeeping

genes in order to provide normalized values for the UKW nucleic acid levels which can be used to provide a fair comparison between the two samples.

Another aspect of the present invention relates to an assay for determining whether pancreatic tumor cells are present in a test sample in which the level of UKW nucleic acid present in the test sample is compared with the level of nucleic acid encoding a housekeeping gene present in the same test sample. Applicants have found that an at least 3-fold greater amount of UKW nucleic acid versus the amount of nucleic acid for the housekeeping gene is indicative of the presence of pancreatic tumor. In such an assay, a control sample is not used and, therefore, there is no need to normalize the values for the levels of nucleic acids measured across samples since only one sample is used. Claim 3 relates to this second aspect of the present invention.

Applicants respectfully submit that the Examiner has misconstrued Example 1. Example 1 **does not** describe the practice of a process according to claim 3. Rather, it describes the practice of a process according to claim 2. As evident in the Example, two cancerous samples were compared with a non-cancerous control sample. The levels of UKW nucleic acids were measured for each sample and compared. To provide for a fair comparison, the levels of nucleic acid encoding a housekeeping gene were also measured and the values for the levels of UKW nucleic acids were normalized therewith. It is, therefore, not the case that Example 1 contradicts claim 3 because it doesn't relate to claim 3 in the first place. It relates to claim 2.

As stated above, the MPEP provides that the Examiner has the initial burden of establishing a reasonable basis to question the enablement provided for the claimed invention. In the present case, applicants adequately teach one skilled in the art how to practice the process of claim 3 by teaching that an at least 3-fold difference in the level of hybridization present in the test sample as compared with the level of nucleic acid encoding a housekeeping gene in the same test sample is indicative of the presence of

pancreatic tumor cells. The sole basis provided by the Examiner for doubting this enablement is that Example 1 allegedly contradicts the practice of the process of claim 3 because it discloses a different process. However, as discussed above, Example 1 was not intended to demonstrate the practice of the process of claim 3 in the first place and instead relates to the practice of the process of claim 2. It is thus not the case at all that it contradicts the aforementioned teaching relating to the process of claim 3. Moreover, if anything, the fact that mRNA levels for housekeeping genes were used to normalize the values measured for UKW nucleic acid is indicative of the fact that the housekeeping gene is not upregulated in pancreatic cancer cells and thus can be used as a control in the process of claim 3. As the sole reason the Examiner provided for questioning the enablement of claim 3 is incorrect and, therefore, not reasonable, the Examiner has failed to meet her initial burden. As there is no reason to doubt the disclosure of the specification, the aforementioned teaching of how to practice the present invention, in the above-recited words of the MPEP, "must be taken as being in compliance with the enablement requirement." The Examiner's rejection is, therefore, respectfully traversed.

The Section 112, Written Description Requirement, Rejections

Claims 1 to 3 were rejected under the written description requirement of Section 112, first paragraph.

Claim 1 was rejected because the specification allegedly does not provide written descriptive support for an assay for determining the presence or absence of pancreatic cancer by detecting the presence of a nucleic acid other than the mRNA which is useful for producing the cDNA consisting of SEQ ID NO: 1. While not acquiescing in the Examiner's rejection, applicants have hereby amended claim 1 to define the mRNA to be detected by the claimed assay as being one which is capable of being used in the

production of the sequence consisting of SEQ ID NO: 1. In view of the above, the Examiner's rejection of claim 1 has been overcome.

Claim 1 was further rejected because the specification allegedly does not provide support for the previously submitted amendment in which the claim was amended to recite the phrase "detecting in the sample mRNA encoding a polypeptide having the amino acid sequence of SEQ ID NO: 2." While not acquiescing in the Examiner's rejection, applicants submit that the above amendment of claim 1 to define the mRNA as being one which is useful in producing the cDNA of SEQ ID NO: 1 overcomes this rejection. Support for this amendment is found in paragraph [0021] of the specification as filed.

In addition, Claim 1 was further rejected because the specification allegedly does not provide support for all possible mRNAs encoding a polypeptide having the amino acid sequence of SEQ ID NO: 2. While not acquiescing in the Examiner's rejection, applicants submit that the above amendment of claim 1 to define the mRNA as being one which is useful in producing the cDNA of SEQ ID NO: 1 overcomes this rejection.

Claim 2 and 3 were rejected because the application allegedly does not provide written descriptive support for the use, as a probe, of any nucleic acid which is complementary to SEQ ID NO: 1 (the Examiner interprets "complementary" to cover sequences which are complementary only in part to SEQ ID NO: 1) or any sequence which is capable of hybridizing under moderate stringent conditions with SEQ ID NO: 1. While not acquiescing in the Examiner's rejection, applicants have hereby amended claims 2 and 3 to more specifically define the probe which is complementary to SEQ ID NO: 1 as being one which is 100% complementary to SEQ ID NO: 1 and to specify that the hybridization conditions with regard to the second set of probes be high stringency. As such, the Examiner's rejection has been overcome.

Claim 2 was further rejected because the specification allegedly does not provide support for the "newly added" recitation of "detecting mRNA encoding a polypeptide having the amino acid sequence of SEQ ID NO: 2" (see item 14 of the Action). It is unclear what the Examiner intends by this rejection because such a recitation was not added to claim 2. In fact, SEQ ID NO: 2 is not mentioned at all in this claim. Further, it appears at the end of Item 14 of the Action that the Examiner alludes to the rejection as applying to claim 3 as well though she has not officially stated that it does. In any event, claim 3 does not mention SEQ ID NO: 2 either. As such, the Examiner's rejection is without basis and is respectfully traversed.

Claim 2 was further rejected because the application allegedly does not provide written descriptive support for the phrase "fluid from pancreatic tumor cells" which was added in a previous Amendment. While not acquiescing in the Examiner's rejection, applicants have hereby amended claim 2 to delete this phrase. In view of the above, this rejection has been overcome.

The Section 112, Second Paragraph, Rejection

Claim 2 was rejected under the second paragraph of Section 112 as being indefinite because the claim does not recite how much greater the level of hybridization in the test sample must be in comparison to the level in the control sample for one skilled in the art to determine that pancreatic tumor cells are present. This rejection has been overcome by the present amendment to claim 2 in which the claim has been amended to recite that an approximately 15-fold to approximately 60-fold difference in the level of hybridization present in the test sample as compared with the level of hybridization present in the control sample is indicative of the presence of pancreatic tumor cells.

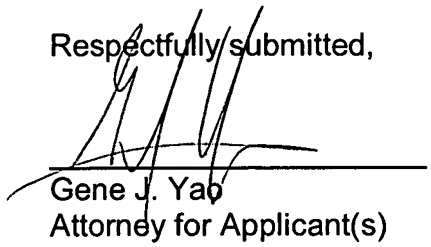
CONCLUSION

The foregoing amendment is fully responsive to the Office Action issued July 11, 2007. Applicants submit that claims 1 to 3, as amended, and claims 13 to 17 are allowable. Early and favorable consideration is earnestly solicited.

If the Examiner believes there are other issues that can be resolved by telephone interview, or that there are any informalities remaining in the application which may be corrected by Examiner's Amendment, a telephone call to the undersigned attorney is respectfully solicited.

The Patent Office is hereby authorized to charge any required fees, including any extension of time and/or excess claim fees, or credit any overpayment, to applicant's Deposit Account 08-2525 as appropriate.

Respectfully submitted,



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